Hunting the Vitamin*

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AN OUTSTANDING event of 1926–27 in vitamin research has been the demonstration of complexity in what we have been wont to designate as Vitamin B or, in Funk's nomenclature, the antineuritic vitamin. Smith and Hendrick [1] in this country probably first produced satisfactory evidence of at least the duality of the complex though Emmett and others had some years before noted the possibility. Goldberger and his coworkers [2] have extended these studies of Smith and Hendrick and shown that one of the vitamin B factors is relatively heat stabile, non-antineuritic but definitely antipellagric. This viewpoint has been confirmed by other workers in both this country and in Europe.

From Java also comes this year the announcement of the isolation of the antineuritic factor in crystalline form, reported by Jansen and Donath.[3]

It is then at least evident that what we have called vitamin B consists of two vitamins and that these factors are distributed in food sources of the vitamin in differing proportion. A food in other words may be a good antineuritic and a poor antipellagric or *vice versa.* It is however still far from certain that what we have called vitamin B is merely dual in nature. The data already obtained however strongly emphasizes the need of chemical fractionation of these factors if we are to learn their rôle in diet and health.

During the past seven years R. R. Williams has actively coöperated with my laboratory in the study of vitamin B fractionation. Independently and in collaboration he has accumulated a vast amount of data involving over 1000 pigeon feeding tests and many rat feeding tests. The detail of this experimentation has an important bearing on both the chemistry and physiology of vitamin B factors and will soon appear in print.

Dr. Ralph Kerr, who developed with Williams and myself the isolation of a crystalline bios (bios 223), has during the past year separated from yeast another substance of chemical homogeneity and

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while his work has not yet reached the point of complete purification of the substance or of chemical designation comparable to what exists for bios 223, the new product (beta bios) is quite different from the first and apparently of greater growth stimulating power.

In a sabbatical leave tour of France and England during the first of this year, I had the opportunity of personally observing the methods and results of Randoin, Besszonof, Drummond, Chick and Peters and other workers in the field.

In view of the above it has seemed to me not out of place to review some of the data now existent concerning the vitamin B complex and especially the work of my own laboratory as it relates to work of other laboratories now studying this problem from the chemical angle.

At the Lister Institute in London, in May, 1927, Dr. Harriet Chick, in collaboration with Miss Roscoe [4] had obtained data apparently fully confirming Goldberger's contention that the yeast vitamin B is composed of an antineuritic factor and an antipellagric factor. Her work makes clear that both of these factors are necessary for continuous growth in rats and that the antipellagric factor is more heat stabile than is the factor which prevents or cures polyneuritis, but it is both misleading and contrary to fact to designate the antipellagric as the growth factor in contradistinction to the antineuritic factor, for so far as her experiments go they show that the rat will decline and die unless both factors are present in suitable proportions. Her studies also show that wheat embryo is much richer in the antineuritic factor than in the antipellagric one, thus putting wheat in the same category as corn in this respect.

It may be recalled here that Goldberger's success in demonstrating the P-P factor (his designation for the antipellagric) lay in his utilization of an alcoholic extract of cornmeal which, like Chick's alcohol extract of wheat embryo, proved relatively poor in P-P but rich in antineuritic. Chick's experiments are however in a way still more conclusive owing to her possessing a source of antineuritic *practically devoid of P-P*. This she owed to the success of Kinnersley and Peters of the Oxford University Department of Biochemistry. In this country we have known for some time that by autoclaving yeast at 120° C. we can destroy its heat labile polyneuritis preventing power without loss of its more heat stabile P-P factor. We have however lacked a preparation that was rich in antineuritic but entirely devoid of P-P. Kinnersley and Peters's "torulin" yeast fraction therefore particularly interested me. Their preliminary method has already appeared in print [5] but Peters has since greatly refined this method and has kindly provided me with details of his present method including his manner of con-

trolling the selective adsorptive power of norite for the antineuritic factor. His present method is briefly summarized below:

SUMMARY OF PETERS AND KINNERSLEY'S PRESENT METHOD OF OBTAINING "TORULIN"

1. Extract partly autolyzed baker's yeast with boiling water. Filter.
2. Treat filtrates with 25 per cent neutral lead acetate. Filter.
3. Treat with baryta to remove gum. Filter and make acid to Congo red with sulfuric.
4. Remove baryta with sulfuric acid. Filter. Make solution pH 2.5.
5. Add mercuric sulfate in sulfuric acid. Filter.
6. Make filtrate pH 7. Add dry purified norite. Filter after 10 minutes' stirring.
7. Re-treat filtrates with additional norite to complete removal of torulin at pH 7.
8. Extract torulin from norite with N/10 HCl on hot water bath.
9. Purify torulin by alcoholic fractionation method after the manner of Osborne-Wakemann.

My interest in this "torulin" fraction and Chick's use of it was further stimulated on my return from Europe by finding that my colleague Williams had in my absence also succeeded in accomplishing a fractionation of the more heat labile part of vitamin B by refinements in the control of the adsorbing power of fuller's earth. Almost coincident with these developments came the announcement by Jansen and Donath of the isolation of a crystalline antineuritic of high potency.

Are Peters's "torulin," Williams's specifically activated fuller's earths, and Jansen and Donath's crystalline antineuritic, identical in character? Unfortunately data are not yet available to settle this point. Peters tells me that he has been unable to make Jansen and Donath's method produce a product such as they describe when he has applied it to his norite fraction. Since however, the method of Jansen and Donath was applied to rice polish extract, Peters's failure may be due to interference with the method by substances present in yeast and absent in rice polish. Peters has also confined his tests for potency to measurements of dosage necessary to cure pigeons sick of polyneuritis in a given time period. He has, so far as I can learn,[8] reported only two observations on the weight restoration or weight-maintaining power of his torulin fraction and in these two cases the birds were cured of polyneuritic symptoms but continued to decline in weight. Jansen and Donath report only a few observations on pigeon weights but imply that their fraction not only cured polyneuritis but also prevented weight loss.

The properties of Williams's preparations are presented in the accompanying Chart I, and will be described much more in detail in his own report of these findings. His preparations used in preventive

TO SHOW THE SPECIFICITY OF WILLIAMS'S PREPARATIONS WHEN USED IN TESTS WITH PIGEONS

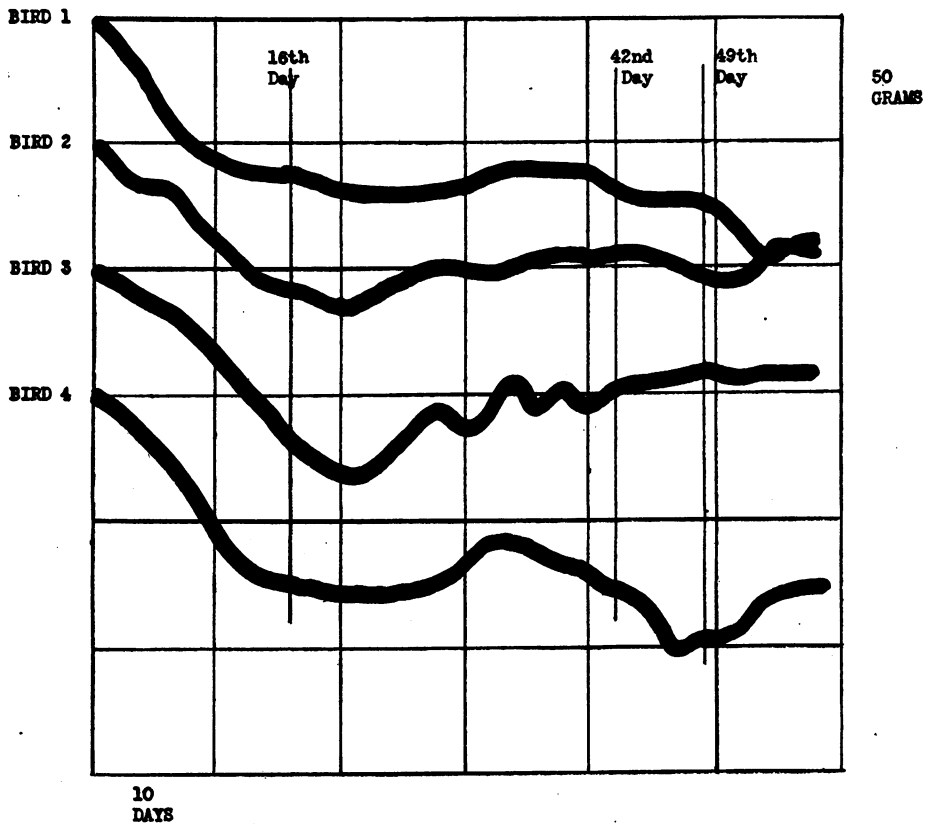


CHART I—*Four adult pigeons were fed on polished rice alone until the 16th day. On the 16th day each bird received 5 mg. of Williams's preparation Y1 and this dosage was continued daily up to the 42nd day. The birds ceased to decline in weight and showed no polyneuritis but failed to return to normal weight. On the 42nd day the dose of Y1 was quadrupled (20 mg. daily) and on the 49th day quadrupled again (80 mg. daily). These increases failed to appreciably restore weight. Addition of autoclaved yeast on the 58th day also failed to restore weight but the birds promptly recovered when fed whole grain or whole dried yeast. Pigeons therefore require what is in Y1 to protect from polyneuritis and to maintain weight but Y1 lacks a factor present in whole yeast and in autoclaved yeast which the pigeon needs. Is this vitamin B3? The heavy line in the chart is the growth curve.*

tests uniformly exert some power toward the restoration of weight or at least to maintaining of weight at a lower level than normal, but in no case or dosage yet tested are they capable of bringing the birds back to the weight they had before the polished rice feeding began. With rats Williams's preparation produces, when used as the sole source of vitamin B in an otherwise adequate diet, a slight amount of growth. Autoclaved yeast alone also stimulates growth at first but a growth that is soon arrested and followed by death from polyneuritis. By combining the Williams preparation with an adequate supply of autoclaved yeast

normal rat growth is obtained. It prevents polyneuritis in both rats and pigeons in doses as low as 5 mg. of activated earth per day.

Chick's work shows that Peters's extract resembles Williams's fraction when supplied to rats, i.e., it is lacking in the heat stabile factor of autoclaved yeast. Seidell's experiments and ours make it doubtful whether the P-P factor of autoclaved yeast is required by pigeons. To date it has been found impossible to restore birds to normal weight by adding autoclaved yeast to the Williams factor in pigeon feeding. Hence in the lack of further data from Peters we know only that his torulin fraction behaves like Williams's fraction toward rats but not that it is identical in bird affecting values. In brief, it is still a question whether the heat labile factors required by pigeons are one or two; whether the vitamin B complex of yeast is composed of two heat labile and one relatively heat stabile* factor, one of each or several of each.

Significant then as are these fractionations in the matter of solving the problem of what vitamin B is, that problem still exists. There is neither time nor place here for further discussion of these points. It will however be immediately evident to the public health worker or dietary adviser that we must have a complete revision of our tests and data on the distribution of vitamin B in foodstuffs and that the preparations described above are going to be valuable tools in this work. Previous tests have taught us the amounts of food considered as source of vitamin B necessary to normal or subnormal rat growth or to pigeon health, but not their antineuritic versus their antipellagric content. I wish then to consider next some of our preliminary work in approaching this problem of differentiating the vitamin fractions.

A year ago I reported to this Association a series of experiments devised to show the vitamin value of the banana.[6] In that report I showed that by the Sherman rat test 8–10 g. of ripe banana per day per rat was necessary to prevent polyneuritis and secure a growth of 20 g. gain in 60 days using 30-day old white rats as test animals. How much antineuritic and how much antipellagric vitamin is present in this quantity of banana? Obviously the gross test of last year shows that both factors are present in banana but fails to differentiate them. With the aid of Williams's preparations and autoclaved yeast we now have tools that enable us to do this. Chart II summarizes the feeding tests to date. In brief, if the antineuritic factor is supplied by an adequate source such as Williams's preparation which is at the same time free of

* It will be noted that we are careful to describe the P-P factor as relatively heat stabile. Ordinary autoclaving of yeast adequate to destruction of its polyneuritis preventing power leaves the yeast antipellagric. An accident in allowing the autoclaving to proceed for a longer time demonstrated that under these conditions the antipellagric power will also disappear. P-P is then capable of heat destruction but far more resistant to it than is the antineuritic fraction.

TO SHOW THE SPECIFICITY OF WILLIAMS'S PREPARATIONS WHEN USED IN TESTS WITH WHITE RATS

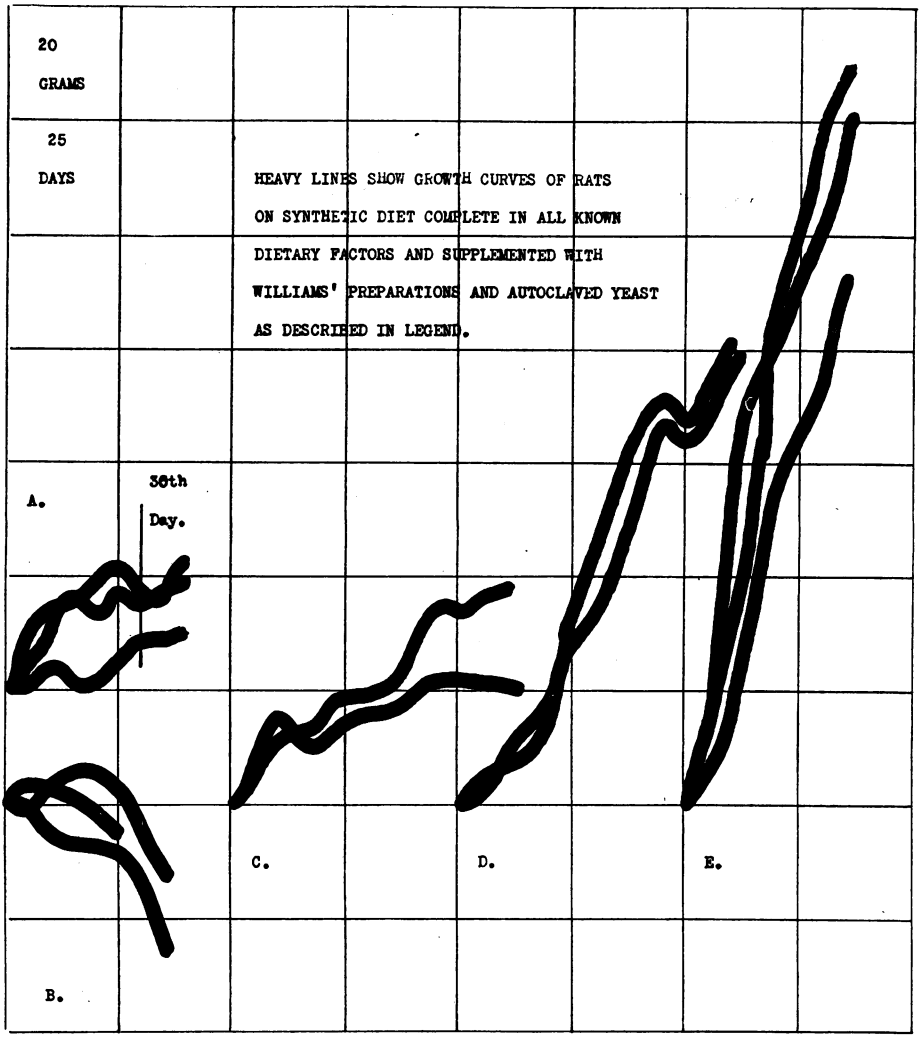


CHART II—*A. Three rats 30 days of age were fed on a vitamin B-free basal diet plus 10 mg. Williams's preparation Y1 daily. On the 30th day the Y1 was quadrupled (40 mg.). A slight temporary gain was not maintained but no symptoms of polyneuritis appeared. Y1 then protects rats from polyneuritis, permits some weight gain but is not adequate for normal growth. B, C, D, E. These four groups of 30-day old rats were fed as follows: Group B received the same basal diet as Group A, plus 1 g. of autoclaved yeast daily. They received no Williams's preparation. They declined in weight and died of acute polyneuritis in 25–40 days. Groups C, D, and E received the same basal diet and autoclaved yeast dosage as Group B. In addition Group C received 3 mg. Williams's Y1 daily, Group D received 6 mg. Y1 daily and Group E 10 mg. Y1 daily. When the rat receives his antipellagric factor in the form of autoclaved yeast and his antineuritic factor in the form of Williams's preparation normal growth results. He apparently needs only vitamins B1 and B2 and does not require the factor B3 essential to the pigeon.*

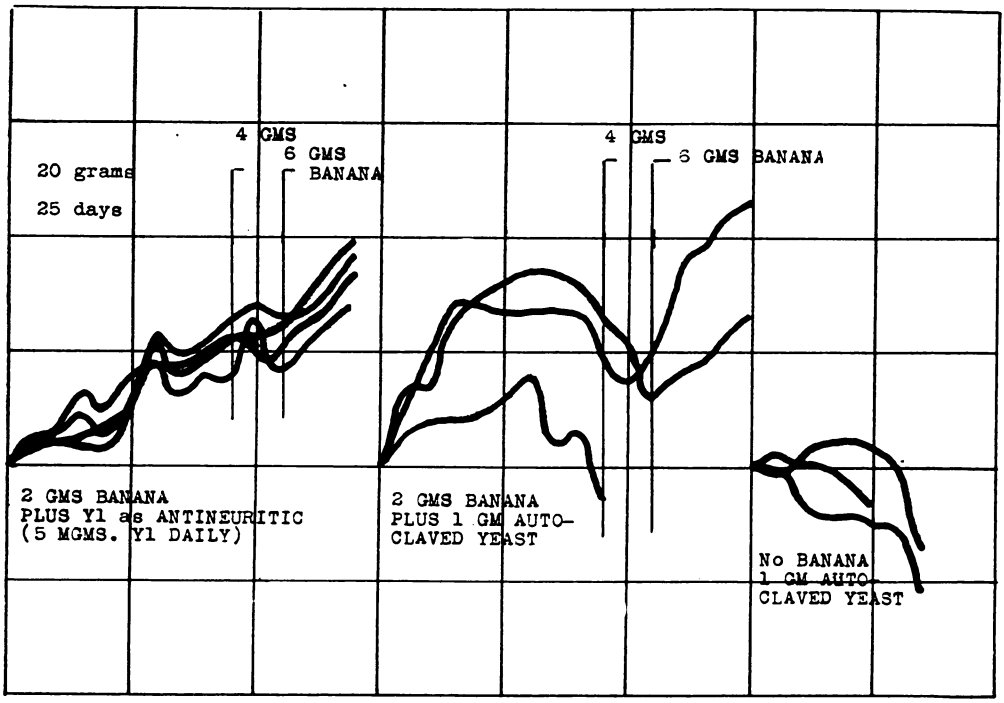
P-P, even 2 g. of banana per rat per day supplies enough of the latter factor to produce better than 20 g. gain in 60 days and 6 g. of banana furnishes enough P-P for nearly normal growth curves. The banana should then be a good antipellagric. On the other hand, if P-P is supplied by autoclaved yeast devoid of antineuritic, rats fail to show an upward growth trend until at least 6 g. per day of banana is added to supply antineuritic. The differentiation of vitamin B in a fruit such as the banana then seems to indicate a better content of antipellagric than of antineuritic. Does this hold true of other fruits? Tests of course will be our only means to the answer, but the tools are now available for the tests.

We have as yet had time to test only one other foodstuff by this method. In our study of the distribution of vitamins in canned spinach, Kohman and I [7] reported some time ago certain observations on its vitamin B content. At the time we noted a marked difference in the behavior of dried raw spinach and dried cooked spinach as a source of vitamin B with an apparent lessened potency of the latter. We did find however that the canned was as good as the home cooked in this respect. In carrying our control experiments we made the discovery that if a rat received *one-third* of his vitamin B requirement in the form of dried yeast, he not only was able to use dried cooked spinach to meet the other two-thirds requirement, but would readily eat enough to bring about this result. We felt at the time that the yeast was a means of stimulating the appetite of the rat for spinach rather than that the spinach was lacking in B. We did however record at the time one experiment of Williams with our dried cooked spinach in which he was unable to prevent polyneuritis in pigeons with a daily dosage of 4.4 g.

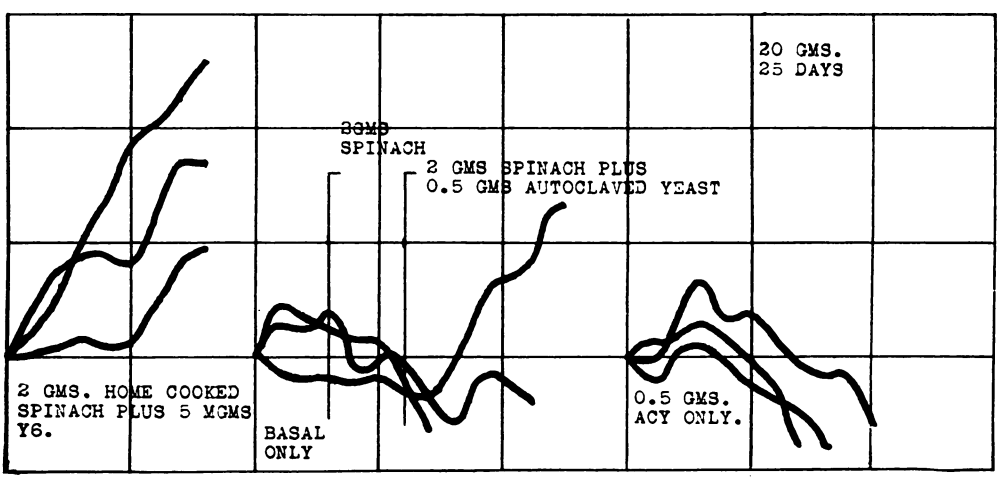
Pigeon and rat testers have frequently reported similar discrepancies in studies of vegetable and fruit sources of vitamin B. We have therefore, as in the case of the banana, begun a series of tests of the vitamin B value of spinach using similar methods and utilizing autoclaved yeast and the Williams preparations in tests. Chart II shows data obtained to date using undried home cooked spinach in this series. Again we find that while the spinach is not devoid of either factor, it is a much better source of the antipellagric than of the antineuritic, and that cooking tends to reduce its antineuritic value.

The purpose of this paper is primarily to show the importance of chemical fractionation methods in progress toward the solution of problems of vitamin behavior. Perhaps these two illustrations have adequately indicated how hunting the vitamin B fractions has been a step toward better dietetic advice and a means to further progress in that line. Since, however, we are not at all sure as yet as to how many

APPLICATION OF WILLIAMS'S PREPARATIONS TO VITAMIN B TESTS ON FOODSTUFFS



TESTS ON RIPE BANANA SHOWING IT TO BE A BETTER ANTIPELLAGRIC THAN AN ANTINEURITIC THOUGH CONTAINING BOTH FACTORS



TESTS ON UNDRIED HOME COOKED SPINACH SHOWING IT TO BE A MUCH BETTER ANTIPELLAGRIC THAN ANTINEURITIC

CHART III—*Since the Williams's preparation Y1 supplies the rat with antineuritic factor only and the autoclaved yeast with antipellagric factor only it is possible with these two substances to determine quantitatively the amount of each kind of factor present in a food stuff. Chart III shows how these factors were used to show that both banana and spinach are richer in antipellagric than antineuritic factor. By giving the rat in combination with an otherwise adequate basal diet enough of either factor to meet his need for that, the value of a foodstuff as supply of the missing factor is measurable.*

vitamins B exist, it is perhaps well to emphasize both their value and limitations. The latter consideration gives point to the urge to greater activity in the field of chemical isolation and before closing this paper I wish to report briefly certain other chemical phases of our vitamin hunt attained during the past year.

Sir James Irvine recently put his reasons for interest in the study of carbohydrates as follows:

> My reflections have convinced me that first importance must be attached to the fact that carbohydrates are essentially the products of natural, as opposed to artificial, synthesis. Within us and around us, through the agency of life, these compounds are being built up and broken down, formed and transformed, finally to be consumed in the fire of metabolism. To study the sugars is, in brief, to study the great molecular channel through which solar energy flows to us. No wonder that the thought of such work makes a powerful appeal to the student of vitalism who is naturally somewhat inclined to turn aside from that aspect of chemistry which deals with purely artificial reactions.

The study of yeast behavior and the factors that control it has for a somewhat similar reason to that advanced by Irvine, always interested the biochemist. The postulation of bioses that function in stimulating yeast growth, much as vitamins stimulate the growth of higher organisms, has held out the hope that by isolation and observation of the behavior of these bioses we might obtain more easily the clue to the method of activity of the vitamins even though, as now seems evident, such bioses do not appear to be of importance in animal nutrition.

Three years ago Kerr, Williams and I [8] succeeded in isolating from yeast a crystalline amino acid that seemed to function as a bios. A later discovery was the fact [9] that the activity of this compound could be completely blocked by substituting for one of its NH_2 hydrogens an additional compound (benzene sulfon chloride) and that this inactive compound became active again when the substituted product was removed and the hydrogen restored by hydrolysis. Such studies seemed to be bringing our hunt closer to localizing the seat of activity of these compounds. However, a series of events has postponed for the time our pursuit of the study of bios 223.

By following our method exactly Roger Williams [10] was able to separate from yeast our crystalline bios or at least a product with the same physical and chemical constants. When he tested the activity of this product on the yeast at his command he reported two results of significance, viz., that the isolated amino acid is not so active as the yeast autolysate from which it is separated and that its stimulative power is confined to certain strains of yeast. His findings are given in part in Table I.

TABLE I

ROGER WILLIAMS'S RESULTS WITH BIOS 223 TESTS

I. 24 hours incubation at 31° C.		II. 48 hours incubation at 31° C.	
Test	Yeast crop in mg.	Test	Yeast crop in mg.
Control (no bios)	1.0	Control (no bios)	1.7
10 mg. yeast autol	2.1	1 mg. bios	2.7
0.5 mg. bios	1.4	1 mg. bios	2.9
0.2 mg. bios	1.6	10 mg. cane molasses	3.3
0.06 mg. bios	1.3	20 mg. cane molasses	4.1

Meanwhile, unaware of Williams's results at the time, our own tests had revealed similar peculiarities as well as other data of interest in the matter of bios behavior. Some of these data are given in Table II.

The results showed conclusively that our bios 223 isolated from yeast autolysate either was not the sole bios or lacked some factor left in the yeast to attain maximum stimulation. The results also strongly suggest that these bioses are not growth catalysts but true yeast foods, the stimulation being directly proportional to the amount of bios present. In view of these results it seemed best to turn for the moment from the study of structure of bios 223 and hunt for another bios in the yeast autolysate. That search has been successful and will shortly be reported in detail by Dr. Kerr. The following brief summary will show how the new product (beta bios) was obtained and in Table III are given a series of comparisons between its behavior as a growth stimulus and bios 223. Chemical analysis indicates homogeneity in fractions obtained by duplication of the isolation method and certain indications as to its structural composition are now available, but it is unlike bios 223 in being very hygroscopic, and we have not yet suc-

TABLE II

SOME OF KERR AND EDDY'S TESTS WITH BIOS 223

Series I. Using 0.1 c.c. yeast autolysate per 10 c.c. Clark's medium					Series II. Using 0.1 mg. bios 223 per c.c. of Clark's medium			
Seedings	A		B		C		D	
	Controls	Yeast tube	Controls	Yeast tube	Controls	Old Bios	Controls	Fresh made bios
c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.	c.c.
0.1	.001	.068	.002	.075	.001	.003	.002	.019
0.2	.004	.067	.004	.081	.004	.006	.006	.022
0.3	.005	.062	.007	.076	.007	.008	.009	.018
0.4	.007	.061	.009	.069	.008	.009	.010	.019
0.5	.008	.065	.009	.073	.009	.010	.010	.018
0.6	.009	.068	.010	.076	.010	.010	.011	.020
0.7	.010	.063	.011	.077	.010	.014	.011	.019
0.8	.011	.064	.012	.068	.011	.013	.011	.017
0.9	.011	.065	.012	.076	.012	.013	.013	.012
1.0	.011	.068	.012	.079	.011	.014	.016	.020

Incubation 48 hours at 31° C. One c.c. seeding means 250,000 cells per c.c.
Results in volumes c.c. per Hopkins tubes after Funk-Dubin method.

ceeded in getting it in crystalline form. Like bios 223, it contains both amino and carboxyl groups.

TABLE III

TABLE SHOWING COMPARATIVE ACTIVITIES OF ALPHA AND BETA BIOSES

Dosage: 0.001 mg. Bioses per c.c. of Roger Williams's culture medium.
Seeding in each case 250000 cells per 10 c.c. medium.
Growth reported in volumes of centrifuged cells after Funk-Dubin method.
Incubation at 31° C. in still tubes.

A. Tests applied to Gebrüde Mayer Yeast (supplied by Fleischmann Co.)

Results at end of	24 hrs.	48 hrs.	72 hrs.
	c.c.	c.c.	c.c.
Control (no bios)	.001	.002	.017
Control (no bios)	.002	.002	.012
Alpha-Bios	.003	.011	.024
Alpha-Bios	.002	.010	.020
Beta-Bios	.008	.013	.031
Beta-Bios	.009	.012	.031

B. Tests applied to Ruppert Brewing yeast (supplied by Ruppert Brewing Co.)

Results at end of	24 hrs.	48 hrs.	72 hrs.
	c.c.	c.c.	c.c.
Control (no bios)	.001	.002	.001
Control (no bios)	.001	.002	.002
Alpha-Bios	.003	.014	.013
Alpha-Bios	.002	.015	.012
Beta-Bios	.002	.017	.019
Beta-Bios	.004	.019	.020

C. Tests applied to Untergarige Hefe K (supplied by Fleischmann Co.)

Results at end of	24 hrs.	48 hrs.	72 hrs.
	c.c.	c.c.	c.c.
Control (no bios)	.001	.002	.002
Control (no bios)	.002	.003	.002
Alpha-Bios	.003	.010	.011
Alpha-Bios	.004	.012	.010
Beta-Bios	.009	.015	.013
Beta-Bios	.004	.018	.016

BRIEF RECAPITULATION OF KERR'S PRESENT METHOD OF SEPARATING ALPHA AND BETA BIOS FROM YEAST AUTOLYSATE

I. Preparation of extract which contains both bioses:
   a. Autolyse brewer's yeast 3 days at room temperature. Filter.
   b. Dilute with equal volume of water and refilter.
   c. Heat filtrate to boiling and discard unfilterable matter.
   d. Stir with 50 g. fuller's earth per l. (750 g. per extract 100 lbs. moist yeast.) This process removes the vitamin B and takes out little bios.
   e. Make filtrate pH 4.7 and stir with iron sol. Discard ppt.
   f. Make filtrate pH 5.3 and use double amount of iron sol. used above. At this pH the iron sol. in suitable quantity removes both bioses. Adsorption complete if stirred and then allowed to stand 30 minutes before filtering. Activated iron sol. further purified by mixing with water, stirring and again filtering.
   g. Obtain bioses from iron sol. by first drying the latter. While still pasty add as little as possible of 30 per cent sulfuric acid. When solution is

nearly complete, dilute with water until sulfuric acid content is not over 5 per cent. Remove iron and sulfate ion with baryta at pH 7. Filter only at this pH. Beta bios is lost if filtered at alkaline reaction.

II. Separation of the bioses from the above extract:
   a. Remove baryta with sulfuric acid and concentrate at 50° to sirupy consistency. Add 95 per cent alcohol and satt. baryta (hot) until alcohol content is 70 per cent and no more baryta gum flocks out. Let ppt. settle. Decant and filter the supernatant fluid. The precipitate now contains the beta bios. The filtrate contains the alpha bios (bios 223).

III. Purification of beta bios:
   a. Stir ppt. with water and filter. Repeat until water filtrate is colorless.
   b. Neutralize filtrates as rapidly as possible with sulfuric and combine.
   c. Make combined filtrates pH 5–6 and filter.
   d. Add hot water solution of silver sulfate and reject ppt.
   e. Add acid mercuric sulfate to filtrate and reject ppt.
   f. Evaporate extract from 100 lbs. yeast to 100 c.c. Add sulfuric to 5 per cent by wt. Precipitate with 20 per cent phosphotungstic acid in 5 per cent sulfuric. Let stand over night and filter. Save ppt. Discard filtrate.
   g. Decompose the phosphotungstic ppt. as follows:
      Dissolve ppt. in as little 80 per cent acetone as possible and add cold 1/3 satt. baryta. When the mixture is free of soluble phosphotungstate evaporate with constant stirring and air blast until free of acetone. Filter and discard ppt. Remove barium quantitatively with sulfuric and concentrate filtrate to sirup by fanning at 30° C. (Compound is very thermo-labile.) Do not attempt to carry this to dryness. Dry the product by stirring in large quantities of acetone until the residue becomes a dry granular yellow powder. Filter the acetone suspension by suction until the last free acetone disappears from the top of the ppt. While the residue is still moist with acetone transfer to a cool dry container and place immediately in vacuum desiccator over fresh sulfuric acid. Remove last traces of acetone suction. Light yellow semi-crystalline powder is beta-bios.

Are there other bioses in yeast? Are these two products similar in function? Are they related in any way in origin? Do they exist in yeast as separate entities or are they parts of a larger molecule split by our fractionation? These and other questions at once arise but the success of the hunt in bringing to light another homogeneous complex of growth stimulating activity has at least multiplied our tools for the study of the chemistry of growth stimulation and perhaps justified delay in the solution of structural problems raised by bios 223 isolation.

I believe that the explanation of the rôle of factors such as vitamins and bioses in nutrition can come only with chemical isolation and perhaps synthesis of the active substances. I feel that the past year has provided distinct encouragement that such isolation is possible, and that we merely await with further patience the refinement of existing procedures to attain the goal. I might have cited equally notable advances in this direction in the study of other vitamins by other

workers. However, in adhering to the rule of the Association that the paper shall deal with original work I have confined my review as much as possible to the developments in my own laboratory with such reference to other work in the field as relates to it.

The significance of this and other work on vitamin structure and behavior perhaps needs no further words of interpretation to workers in public health fields. The true student of the science of nutrition, however, often appears to a disadvantage in the rôle of adviser on dietetic problems due to his consciousness of unsolved problems, an inhibition entirely lacking in the dogmatic food faddist. Perhaps then it is permissible to emphasize a bit the need of such inhibitions and the problems that still exist unsolved to encourage the public health worker to continue to be cautious rather than dogmatic in his advice.

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Paris Has New Type of Open Air School.

A NEW type of open-air school, sponsored by Prof. Alfred Binet, co-inventor of the Binet-Simon Intelligence test, has been opened recently in a thickly populated district of Paris.

The purpose of this school is to provide instruction for each child not according to his age, but according to his physical and mental abilities. Each pupil is examined by a physician at the time of admission; is given a Binet-Simon test; and is then assigned to a grade in accordance with the findings of the examination. The examination is repeated every 3 months, and the child is promoted to a higher grade or left in the same, according to the findings.—*La Pediatria,* Naples, Oct. 15, 1927. p. xxvii.